

RCE Amendment and Response
 Application Serial No. 09/889,687
 Attorney's Docket No. 26979-0002 C1

REMARKS/ARGUMENTS

Claims 23-31 are in this application, claims 1-11 and 19-20 having been canceled in a previous Response, and claims 12-18 and 21-22 have been canceled in this Response.

New composition claims 23-27 correspond to claims 12-16, and new method claims 28-29, and 30-31 correspond to method claims 17-18 and 21-22. The table below shows the correlation of the composition and method claims. New claim 23 limits the definition for X_4 to " $-\text{CH}_2\text{O}$ " and therefore, the amendment necessitates the deletion of the proviso to non-claimed subject matter. In addition, the definition for B, C, D, or E in claim 23 was amended to delete reference to X_4 for unclaimed subject matter; i.e. where " X_4 is H, $-\text{CH}_3$ or CH_2N_3 ".

Dependent claim 27 has also been amended to reflect the limited scope recited in claim 23.

In addition, claims 23-25 have been amended to 1) segregate protecting groups that corresponds to hydroxyl and amino protecting groups and 2) delete species of protecting groups that are already covered by the genus; for example, where the genus of "carbonates" include the species "Alloc, Fmoc, Troc, ...", these species have been deleted.

New claim	Old claim	Note
	1-11	canceled
23	12	composition
24	13	" "
25	14	" "
26	15	" "
27	16	" "
28	17	method
29	18	" "
	19	canceled
	20	canceled
30	21	method
31	22	" "

Claims 12-18, 21 and 22 were rejected under 35 USC 112, second paragraph, and under 35 USC 102(b). In view of the amendments filed herein, the rejections as applied to new claims 23-29, 30 and 31 are respectfully traversed.

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No new matter is added by the new claims. All amendments have been made solely to facilitate the prosecution of the present application, and without acquiescence in any of the rejections and without prejudice to future prosecution of canceled subject matter in this or in continuation or divisional cases.

The 35 USC 112, ¶2 rejection:

Claims 12-18, 21 and 22 were rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regard as the invention. The rejection corresponds to new claims 23-29, 30 and 31, respectively.

In particular, the Examiner objected to:

(A) The term "substitution" or "substituted" in all occurrences in which it appears where "it fails to articulate by chemical name, structural formula, ... requisite to identifying the compound of matter claimed."

Applicants have deleted the term "substitution" or "substituted" in all occurrences in which it appears, primarily in claim 23. In view of this amendment, the objection is rendered moot, and the Examiner is respectfully requested to reconsider and withdraw the present objection.

(B) "The phrase, in claim 12, "an orthogonally protected monosaccharide" is not defined by the claim, the specification does not provide a standard for ascertaining the claim, ... and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." The Examiner suggests that Applicants set forth the identity of the orthogonally protected monosaccharide.

As it applies to new claim 23, Applicants have explicitly recited the members of the protective groups for the orthogonally protected monosaccharide. Explicit support for the protecting groups may be found in the application as filed on page 5, lines 25-34, page 6, lines 1-36, and page 7, lines 1-26.

Claim 23 having been amended, the rejection is moot as to this Claim.

(C) The term "sets" of protecting groups are not defined in all occurrences renders the claims in which it appears indefinite.

Applicants have deleted all references to the term "sets" as "protecting group sets" (Claims 23, 24, and 25); and "an orthogonal set of", "members of set 1" and "orthogonal sets" (Claim 27). Applicants have either deleted any reference to the term "set" where relevant or explicitly recited the members of the protective group sets for the orthogonally protected monosaccharide. In view of these amendments, the objection is rendered moot as to claims 23, 24, 25, and 27.

(D) Claim 17 is rejected as being incomplete for omitting essential steps of the synthesis, such omission amounting to a gap between the steps. According to the Examiner, the steps in the glycosylation reaction are missing.

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As the rejection is applied to new claim 28, the glycosylation step is a single step chemical transformation that converts (or couples) a carbohydrate having a leaving group at the anomeric center with another compound to form a carbohydrate with a different group at the anomeric center. Examples of such on-step process is shown, for example, in the present application for the conversion of compound 36 to 37 (page 33), the conversion of compound 11 to 43 (page 38), and also in Yamada et al (page 5) with the glycosylation of compound 2 and 5 to form compound 6. Because the glycosylation reaction is a single step process, there are no other "essential steps" that can be omitted from the glycosylation reaction.

In view of the above, Applicants respectfully request that the Examiner reconsiders the rejection of claim 28.

(E) The use of the terms "A-E" in all the occurrences is vague and indefinite. The term "A-E" does not define a chemical structure or chemical formula in the claim.

The term "A" as recited in claim 23 is clearly defined as "a leaving group selected from the group consisting of -SR; where R is alkyl," Therefore, the term "A" is not vague and indefinite.

The terms "B, C, D and E" are also defined in claim 23 as "selected from protecting groups which can be cleaved ...". In addition, claim 23 has also been amended to explicitly define the specific protecting groups with chemical formulae or common names, and are listed as members of a Markush group.

Claim 23 having been amended to define the specific members of the protecting groups for B, C, D and E, the rejection is also moot as to this claim. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

The 35 USC 102 rejection:

The Examiner rejected claims 12-18, 21 and 22 under 35 USC 102(b) as being anticipated by Yamada et al (EP 578,112). In particular, the Examiner states that Yamada et al disclose a monosaccharide derivative of Formula II where A is a leaving group at the anomeric center represented by the group -SR; compound 1, page 5; compound 33 on page 8, compound of formula II on page 7. In addition, pages 13 and 14 (Examples 1 and 2) discloses a method of synthesis of glycoconjugates of thio- β -D-glucopyranoside; and claims 5 and 7 discloses a method of synthesis of a disaccharide of formula II from thioglycoside.

The examiner further notes that "in the absence of the defined protecting group sets 1, 2, 6 and 8 and terms A-E in claims 12-18, 21 and 22, the Yamada et al reference is encompassed by the applicants claims."

As the rejection is applied to claims 23-29, 30 and 31, the rejection is respectfully traversed.

First, Applicants submit that the compounds in Yamada et al are not orthogonally protected monosaccharide building blocks as claimed in the present invention. As defined in the present application (page 2, lines 19-20) and as supported generally throughout the application,

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"orthogonal protection" of functional groups or "the principle of orthogonal stability requires that only those protecting functions should be used that can be cleaved under different reaction conditions without affecting the other functions present."

Yamada et al disclose and claim compounds of formula II, for example, having four identical OBz (O-benzyl) groups on a single disaccharide. These four identical OBz groups cannot be considered to be independently stable with regard to the selective removal of a single OBz group without cleaving the other OBz protecting groups. That is, the disaccharide compounds are not orthogonally protected because a specific protecting group of a hydroxyl (OH) group, such as two or more Bz groups as protecting groups for two or more OH groups, cannot be selectively cleaved without affecting the other hydroxyl groups that is also protected by another Bz group.

Yamada et al also disclose the compound of formula III having a free hydroxyl group, and a phthalimido, benzyl, and MPM protecting groups that are also not orthogonally protected because when R₂ is "Bn", formula III has two benzyl groups that cannot be selectively deprotected. In addition, the nature and type of protecting groups disclosed in formula III are not the orthogonally protected groups for the compound of the present invention as recited in claim 23.

Claim 23, as presently amended from claim 12, further defines that the orthogonal groups B, C, D, and E of the present invention are different and can be cleaved orthogonally in any order "such that the cleavage conditions do not compromise the stability of the other protecting or functional groups on the monosaccharide building block." The disaccharide of formula II as disclosed by Yamada et al (page 9) shows four exactly same benzyl protecting groups on a single compound that can not be cleaved orthogonally as taught in the present invention.

Similarly, Example 1 shows the formation of the disaccharide 6 containing two identical "Bz" and "Bn" protecting groups on the same compound and therefore are the same and cannot be cleaved selectively. In addition, the precursor compounds 1-5 have either two of the same hydroxy protecting groups or a single protecting group that protects two adjacent hydroxy groups (the isopropylidene in compounds 1 and 2, and benzylidene in compounds 3 and 4), and therefore, one protected hydroxyl group cannot be selectively cleaved without the concurrent deprotection of the other.

Therefore, Yamada et al do not disclose the orthogonal protecting groups of the present invention that are different and can be cleaved orthogonally. Withdrawal of the rejection is respectfully requested.

Applicants enclose a recent article from H. Kunz et al. noting that the state of the art for the selective manipulation of protecting groups for carbohydrate synthesis has heretofore not yet been discovered until disclosed herein with the present invention. In fact, Kunz et al. state "[s]o far it has not been feasible to selectively remove an individual protective group from any arbitrary position, whilst leaving the protective groups on the other positions untouched." U. Hunger, J. Ohnsmann, and H. Kunz, *Angew. Chem. Int. Ed.* 2004, 43, 1104-1107; see page 1104, second column.

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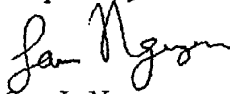
Conclusion

For the reasons given above, Applicants submit that the claims as presently amended are definite under 35 USC 112, ¶2, are not unpatentable under 35 USC 102(b) over Yamada et al, and all pending claims are in condition for allowance.

Re-examination and allowance of the claims are respectfully requested.

Please charge any fees, including any additional fees for extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney's Docket No. 26979-0002 C1). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,



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